Amendments to the Specification:

Please delete the title, beginning before line 1, and replace with the following title:

Methods of Labelling Bio-Organic Molecules

Please amend the paragraph, beginning at line 14, on page 21 as follows:

Preparation of human metaphase chromosomes was performed as described by Wiegant et al. Chromosomes from normal human individuals as well as from *in vitro* cultured JVM-2 cells were used. Probes for all chromosomes were obtained from CYTOCELL ® ~~Cytocell~~, UK. All probe DNA was amplified by DOP-PCR to generate a set of painting probes for all 24 human chromosomes.

Please amend the paragraph, beginning at line 14, on page 22 as follows:

Second, all chromosome-specific painting probes were fluorescently labelled according to table 2 by mixing 30 µl of the listed ULS compounds (or mixtures thereof) with 1 mg of chromosome-specific painting probe DNA (all from CYTOCELL ® ~~Cytocell~~) using DEAC-ULS (26.7 µM), Cy3-ULS (20 µM) and Cy5-ULS (13.3 µM) in a final volume of 100 µl of water. In case probes were labelled with mixtures of two different ULS-compounds, the ULS-compounds were first mixed in the desired ratio before the probe DNA was added. After 15 min incubation at 65°C, the labelled probes were purified on Qiagen quick spin columns (Qiagen Inc., Valencia, CA, USA). The labelled probes were eluted from the Qiagen columns using 100 µl of 10 mM Tris.HCl pH 8.5. Prior to the hybridisation, fluorescent ULS-labelled probes where combined in amounts as indicated in the right column of Table 2 together with the 100 µl of dig-ULS labelled probe mixture from the first step. This probe mixture was then ethanol precipitated in the presence of 10 x excess low molecular weight fish sperm DNA (Boehringer Mannheim), and 3 x excess human C_0t1-

DNA (Gibco, BRL) (an alternative method for suppression of repetitive sequences is presented below). Thereafter the probe mixture was dissolved in 10 µl 50% deionized formamide, 2xSSC, 50 mM sodium phosphate pH 7, 10 % dextran sulfate. This 10 µl of probe mixture was used as hybridisation solution.

Please amend the paragraph, beginning at line 25, on page 23 as follows:

After a 10 min post-hybridisation wash in 2xSSC/0.1% TWEEN 20™ (Polysorbate 20) ~~Tween 20~~ at 37°C to remove the coverslips, the slides were washed 2 x 5 min in 50 % formamide, 2XSSC, pH 7 at 44°C. This was followed by 2 washes (5 min each) in 0.1xSSC at 60°C and a 5 min wash at RT in TNT (0.1M Tris.HCl pH 7.4, 0.15 M NaCl, 0.05% TWEEN 20 ™ (Polysorbate 20) ~~Tween 20~~). The DIG-ULS labelled probes were detected with a mouse monoclonal antibody against digoxin (Sigma) followed by a rabbit anti mouse antibody conjugated to FITC (Sigma). Chromosomes were counterstained with DAPI. The slides were embedded in VECTASHIELD® ~~Vectashield~~ (when enzymatically labelled probes were used) or CITIFLUOR® ~~Citifluor~~ (Agar, Stansted, UK) (when chemically labelled probes were used) prior to microscopical evaluation.

Please amend the paragraph, beginning at line 6, on page 24 as follows:

Digital fluorescence imaging was performed using a LEICA® ~~Leica~~ DM-RXA epifluorescence microscope (LEICA® ~~Leica~~, Wetzlar, Germany) equipped with a 100-W mercury arc lamp and computer controlled filter wheels with excitation and emission filters for visualisation of DEAC, Fluorescein, Cy3 and Cy5, using HQ-FITC, Pinkel set plus SP 570, HQ-Cy3, HQ-Cy5 and DEAC filter (CHROMA TECHNOLOGY CORP ®) ~~(Chroma Technology)~~ respectively. DAPI was excited with UV light using block A. A 63x objective ((N.A. 1.32, PL APO, LEICA® ~~Leica~~) was used.
Image acquisition and analysis was performed on a CYTOVISION® ~~Cytovision~~ workstation (Applied Imaging, Sunderland, UK). This system consists of a PC (PENTIUM® ~~Pentium~~

133MHz processor, 24Mb Ram, 2.1 Gb disc and 17" display) interfaced to a Coolview camera (Photonic Science). The camera has thermo-electric cooling, which allows on chip integration up to circa 30 seconds. Images are digitised in an 8-bit 768 x 512 image format.

Please amend the paragraph, beginning at line 26, on page 37 as follows:

Procedures:

I. Multi-colour FISH staining of human chromosomes

Preparation of human metaphase chromosomes was performed as described by Wiegant et al (1993). Chromosomes from normal human individuals as well as from *in vitro* cultured JVM-2 cells were used. Probes for all chromosomes were obtained from CYTOCELL ® ~~Cytocell~~, UK. All probe DNA was amplified by DOP-PCR to generate a set of painting probes for all 24 human chromosomes.

Please amend the paragraph bridging pages 39 and 40 as follows:

After a 10 min post-hybridisation wash in 2xSSC/0.1% TWEEN 20 ™ (Polysorbate 20) ~~Tween 20~~ at 37°C to remove the coverslips, the slides were washed 2 x 5 min in 50 % formamide, 2XSSC, pH 7 at 44°C. This was followed by 2 washes (5 min each) in 0.1xSSC at 60°C and a 5 min wash at RT in TNT (0.1M Tris.HCl pH 7.4, 0.15 M NaCl, 0.05% TWEEN 20 ™ (Polysorbate 20) ~~Tween 20~~). The DIG-ULS labelled probes were detected with a mouse monoclonal antibody against digoxin (Sigma) followed by a rabbit anti mouse antibody conjugated to FITC (Sigma). Chromosomes were counterstained with DAPI. The slides were embedded in VECTASHIELD® ~~Vectashield®~~ (when enzymatically labelled probes were used) or CITIFLUOR® ~~Citifluor®~~ (Agar, Stansted, UK) (when chemically labelled probes were used) prior to microscopical evaluation.

Please amend the 2nd paragraph on page 40 as follows:

V. Digital imaging microscopy

Digital fluorescence imaging was performed using a LEICA® ~~Leica~~ DM-RXA epifluorescence microscope (LEICA® ~~Leica~~, Wetzlar, Germany) equipped with a 100-W mercury arc lamp and computer controlled filter wheels with excitation and emission filters for visualisation of DEAC, Fluorescein, Cy3 and Cy5, using HQ-FITC, Pinkel set plus SP 570, HQ-Cy3, HQ-Cy5 and DEAC filter (CHROMA TECHNOLOGY CORP.®) (~~Chroma Technology~~) respectively. DAPI was excited with UV light using block A. A 63x objective [[(]](N.A. 1.32, PL APO, LEICA® ~~Leica~~) was used.